REMARKS

The Present Invention

The claimed invention is directed to methods for modifying the genotype or phenotype of a plant, preferentially in plant seed tissue, by transforming a plant with a DNA construct comprised of *i*) a transcriptional initiation or promoter region from a gene of a *Brassica* plant that is preferentially or specifically expressed or regulated in plant seed tissue; and *ii*) a DNA sequence of interest other than the coding sequence native to that gene.

The Pending Claims

Prior to entry of the above amendments, Claims 17-62 are pending. Claim 17 is directed to a method for obtaining a plant having a modified phenotype. Claims 18, 27, 52-53 and 62 are directed to a method for altering the phenotype of plant seed tissue as distinct from other plant tissue. Claims 19-26, 43-45 and 49-51 depend from either Claim 17 or 18. Claims 28-33 are directed to a method for modifying the genotype of a plant to impart a desired characteristic to seed as distinct from other plant tissue. Claims 34-38, 46 and 47 are directed to a method for modifying transcription in seed tissue as distinct from other plant tissue. Claims 39-41 are directed to a method to selectively express a heterologous DNA sequence of interest in seed tissue as distinct from other plant tissue. Claims 42 and 61 are directed to a method for obtaining a plant which produces at least one seed having a modified phenotype. Claim 48 is directed to a method to selectively express a heterologous DNA sequence of interest in plant seed tissue as distinct from other plant tissue. Claims 54-60 depend from either Claim 42 or Claim 53.

Advisory Action

Applicants submission of 15 November, 2000 was not intended as a response to the Final Rejection mailed 4 October, 2000. With this submission, Applicants requested correction of several errors on the filing receipt and removed the priority claim to application

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serial no. 06/692,605 in the specification and on the filing receipt. In view of the change in the priority claim, Applicants also provided a new Inventor Declaration.

The Office Action

Claim 39 remains in error.

Claim 49 is rejected under 35 USC 112, first paragraph, for failing to fulfill the enablement requirement.

Claims 17-41, 43-48, 49-52 and 61-62 are rejected under 35 USC 112, first paragraph, for failing to fulfill the written description requirement.

Claims 17-41, 43-48, 50-52 and 61-62 are rejected under 35 USC 103(a) as unpatentable over Zambryski taken with Sengupta-Gopalan.

Claims 20, 33, 38 and 41 remain rejected under 35 USC 103(a) as being unpatentable over Zambryski taken with Sengupta-Gopalan and further in view of Pedersen.

Claims 17-41, 43-48, 50-52 and 60-62 are rejected under 35 USC 103(a) as being unpatentable over Hall (5,504,200) taken with Sengupta-Gopalan.

Claims 20, 33, 38 and 41 remain rejected under 35 USC 103(a) as being unpatentable over Hall taken with Sengupta-Gopalan and further in view of Zambryski and Pedersen.

Amendments

Applicants have amended Claims 17, 18, 23, 28, 34, 39, 46, 48, 52, 61 and 62 to recite that a gene from a *Brassica* plant is the source of the transcriptional initiation region. Support is found in Examples 2-5 on pages 35-62 and on page 15, lines 18-21 of the specification.

Claim 49 was amended to become a product by process claim. Support for amending Claim 49 is found on page 13, lines 14-18.

Applicants have made the above amendments following the suggestions made by the Examiner in the present official action (i.e. page 5, 1st paragraph and page 6, 2nd full

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paragraph). Applicants have amended the claims strictly in the interest of achieving a Notice of Allowance. The amendments were not made earlier due to inadvertent oversight.

Applicants believe that no new matter has been added by any of these amendments and therefore respectfully request the Examiner to enter them.

Response

The Examiner's specific objections and rejections are reiterated below as small indented bold print, followed by Applicant's response in normal print.

Objections

Claim 39 remains in error as stated in the last office action [Errors appear in Claim 39 where --and-- should be inserted before "a"].

Applicants have amended Claim 39 to correct the typographical error.

Rejections

35 U.S.C. § 112, first paragraph.

Claim 49 (newly submitted) is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention with respect to a cruciferin promoter, as stated in the last office action for claim 42.

Applicants urge that the enablement rejection with regard to the cruciferin promoter is improper, given the teaching in the specification that Simon et al (1985) identified cruciferin cDNA clones from *Brassica napus*, the identification of cruciferin cDNA clones from radish by Laroche-Raynal et al (1986) as evidenced by an Abstract appended to the amendment of 28 June 2000, the ability of Sjodahl et al (1995) to elucidate the fine structure of the *Brassica napus* cruciferin gene promoter directly upstream of the coding region as evidenced by an appended Abstract, the high level of skill in the art, the disclosure in the specification of the identification of promoters from the upstream of three other *Brassica* genes, and the ability of Sengupta-Goplan et al cited by the Examiner to obtain seed-specific promoter function from a directly upstream region of the phaseolin gene.

The Examiner maintains that Laroche-Raynal et al is drawn to a different plant species (for which the instant specification provides no genomic or cDNA clones) and was not cited in the instant specification, while the actual cDNA of Simon et al briefly mentioned in the paragraph bridging pages 62 and 63 was not further elucidated in the specification. Therefore, the instant specification does not provide one skilled in the art the starting materials from which to isolate a *Brassica napus* cruciferin promoter. See *Genentech* cited in the last office action. With regard to Sjodahl et al, see In re Glass,

181 USPQ 31, 34 (CCPA 1974), which teaches that references published after the filing date of an application may not be relied upon for the enablement of the specification.

Applicants respectfully traverse the rejection of Claim 49 under 35 USC 112, for all the reasons made of record for Claim 42 in the response submitted 21 June, 2000. Applicants disagree with the Examiner's position, but in the interest of furthering prosecution, have amended Claim 49 to recite the demonstrated method by which the cruciferin promoter would be obtained (*see* for example, Example 3 on pages 51 and 52). The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. MPEP 2164.01(a). Examples 3-6 on pages 51-63 of the specification provide detailed guidance to the ordinarily skilled artisan regarding how to isolate and use a 5'-flanking region of a gene of a *Brassica* plant that is preferentially expressed in plant seed tissue when starting with the cDNA sequence of the gene. In fact, by knowing the cDNA sequence of the desired gene such as cruciferin at the outset, the skilled artisan is given a head start; in Examples 3-5, cDNA clones were first isolated from cDNA libraries. To carry out the methods of Claim 49, the skilled artisan would follow the explicit protocols detailed in Examples 3-6 using an already known cruciferin cDNA sequence published by Simon, *et al* to isolate the 5' flanking region from genomic DNA. By following Applicants' guidance, the skilled artisan could reasonably expect success without undue experimentation. Contrary to the Examiner's expressed concerns that "the existence of directly upstream tissue-specific promoters is unpredictable" (page 7, 3rd full paragraph, paper 8), the transcriptional initiation region for the cruciferin gene resides predictably in the immediate 5' flanking region. Applicants explicitly stated that their intent in submitting the abstract of Sjodahl *et al.* with the response of 21 June, 2000 was to demonstrate the operability of the invention. The work of Sjodahl *et al.* demonstrates the correctness and operability of Applicants' thinking, that there is reasonable predictability in the art, and that the skilled artisan could reasonably expect success in applying the processes outlined in Examples 3-5 to isolating a *Brassica* cruciferin promoter.

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Applicants respectfully assert that the Examiner cites *Genentech Inc. vs. Novo Nordisk* out of context. In this case, the Genentech, Inc. patent no. 5,424,199 was considered non-enabling for the "fact that *no one had been able to produce* any human protein via cleavable fusion expression as of the application date of patent" (page 1001, paragraph 4, emphasis added). In the present specification, the invention resides in methods of using a promoter that preferentially directs transcription in seed tissue. The process of identifying and isolating a promoter region from a gene that is preferentially expressed in seed tissue is described in great detail for four embodiments using molecular biology techniques well-known to those in the art. Furthermore, the '199 patent was deemed to be without disclosure of specific starting material or of any of the conditions under which a process can be carried out. In the instant case, both starting material and conditions are provided: the conditions for carrying out a process for identifying and isolating a promoter from a cDNA sequence are fastidiously provided for four embodiments and the specification teaches that the starting material can be the cruciferin cDNA disclosed by Simon *et al*. One skilled in the art would know to consult the cited Simon manuscript for the published cruciferin cDNA sequence, that was already in the public domain. Applicants are not required to disclose what is already known in the art. The disclosure that a cruciferin promoter is a further realistic embodiment must be viewed as more than "a mere germ of an idea" when properly considered in the context of the detailed guidance provided in Examples 3-5.

Applicants respectfully affirm that the enablement to allow one of skill in the art to carry out a method of obtaining a plant with produces at least one seed having a modified phenotype or of altering the phenotype of plant seed tissue as distinct from other seed tissue using a transcriptional initiation or a promoter region from a *Brassica* cruciferin gene resides in the detailed processes exemplified for napin, ACP and EA9 promoter regions in Examples 3-6 on pages 35-63 of the specification. Because the cDNA sequence for cruciferin was a part of the public domain, the starting materials to isolate a cruciferin promoter were also available to one skilled in the art. Applicants fastidiously teach how to isolate a promoter from a cDNA sequence. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

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Claim 17-41, 43-48 and new claims 49-52 and 61-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, has possession of the claimed invention, as stated in the last office action for claims 17-48.

Applicants urge that the written description rejection is improper, given the failure of a particular promoter to be essential to the claimed method, Example 18 of the "Revised Interim Written Description Guidelines Training Materials" drawn to method claims, and the failure of the case law cited by the Examiner to deal with method claims.

The Examiner maintains that the instant claims differ from those of Example 18 of the Guidelines. In Example 18, the novelty resided in the transformation of a particularly claimed *single* fungal species, wherein any gene encoding any protein interest could be employed. Thus, the claim scope was commensurate with what was described in the specification. In the instant situation, claim 49 specifically claims a promoter that was neither obtained nor described by the instant specification. Furthermore, the remaining claims are broadly drawn to any seed-specific or seed-preferential promoter from any of a multitude of plant species, wherein said seed-specific or seed-preferential promoter type is in fact crucial to the claimed invention, while the instant specification only demonstrates the isolation and description of three promoters from the single species of *Brassica napus*. Thus, the instant situation involves a method requiring particular products (promoter) which are essential to the claimed invention, wherein the description of these products in the specification is not commensurate with the claim scope.

With regard to method versus composition claims, the Examiner noted that the Revised Guidelines encourage reliance upon the case law cited by the Examiner, and do not prohibit the application of written description rejections to method claims in general.

Applicants respectfully traverse the rejection of Claims 17-41, 43-52 and 61-62 under 35 USC 112, first paragraph for all the reasons already made of record in the response submitted on 21 June, 2000. The present application is a continuation of USSN 08/105,852, filed 10 August, 1993, now USPN 5,753,475. Claims 17-42 were part of the originally filed '852 application. Therefore, these claims by definition are part of the specification, establish conception of the claimed invention for the instant application, and meet the written description requirement. MPEP 608.01(l). Also, subsequently added Claims 43-62 are not any broader than originally filed Claims 17-42, and in fact incorporate the language of the originally filed claims.

Applicants do not agree with the Examiner's position, but have amended independent Claims 17, 18, 23, 28, 34, 39, 46, 48, 52, 61 and 62 to recite a gene from a *Brassica* plant in the interest of furthering prosecution. Applicants respectfully maintain that these independent claims were patentable before introducing the present amendments, and intend to prosecute them in a continuation application.

The Examiner communicates the scope of claims he considers to meet the Written Description requirement on pages 5 and 6 of paper 14. To clarify what the Examiner states on page 5, 1st paragraph and page 6, 2nd paragraph of paper 14, the instant specification demonstrates the isolation of *four* promoters from both *Brassica napus* and *Brassica campestris* species. (1) A *Brassica napus* napin promoter is demonstrated in Example 2 on pages 35-37. (2) A *Brassica campestris* napin promoter is demonstrated in Example 3 on pages 51-54. (3) An ACP promoter from *Brassica campestris* is demonstrated in Example 4 on pages 55-59. (4) An EA9 promoter from *Brassica campestris* is demonstrated in Example 5 on pages 59-62. Applicants respectfully assert that the processes successfully demonstrated in Examples 2-5 of the instant specification show reduction to practice and necessarily convey possession of methods for using promoter regions from genes of a *Brassica* plant that are preferentially expressed in seed tissue together with a non-native coding sequence. The Examiner suggests on pages 5 and 6 of paper 14 that Applicants are in possession of (by demonstrating the isolation and description of) three seed-preferential promoters from the single species of *Brassica napus*, but Examples 2-5 demonstrate the isolation and description of *four* seed-preferential promoters from *two Brassica* species. Therefore, Applicants respectfully assert that the specification is commensurate with the presently claimed methods utilizing promoters from genes of a *Brassica* plant that are preferentially expressed in plant seed tissue together with a non-native coding sequence.

With regard to Claim 49, Applicants do not agree with the Examiner's position, because Examples 2-6 of the specification clearly conveys possession of a method for obtaining a plant which produces at least one seed having a modified phenotype by transforming a host plant cell with a construct comprising a promoter obtained from a cruciferin gene. As stated above, Examples 2-5 fastidiously demonstrate a process for identifying and isolating a promoter using a cDNA sequence as starting material, and Example 6 teaches that a published cruciferin cDNA sequence can serve as starting material. In the interest of furthering prosecution, Applicants have amended Claim 49 to recite the process by which the cruciferin promoter is obtained (*Fiers v. Sugano* 25USPQ2d, 1601). In Examples 2-

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17, on pages 35-79 Applicants provide six working examples (also for the 2A11 and polygalacturonase promoters) that demonstrate the consistent success of this promoter identification process, and the Sjodahl reference cited above and in the June 21, 1998 response shows that this process is applicable to a cruciferin gene.

For all the foregoing reasons, and the reasons outlined in the response submitted June 21, 2000, Applicants respectfully maintain that the specification is commensurate with the claimed methods utilizing promoters from genes of a *Brassica* plant that are preferentially expressed in plant seed tissue together with a non-native coding sequence. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

35 U.S.C. § 103(a)

> **Claims 17-32, 33 (amended), 34-37, 38 (amended), 39-40, 41 (amended), 43-48 and new claims 50-52 and 61-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zambryski *et al* taken with Sengupta-Gopalan *et al* as stated in the last office action for claims 17-32, 34-37, 39-40 and 43-48.**
>
> **Applicants urge that the rejections of the claims under 35 USC 103 over Zambryski et al taken with Sengupta-Gopalan et al are improper, given the failure of either reference to teach or suggest plant transformation with a construct comprising a tissue-specific promoter and a heterologous coding sequence, the failure of Sengupta-Gopalan et al to identify the promoter sequence, and the failure of additionally cited references in the second rejection to cure the deficiencies of the prior two references.**
>
> **The Examiner maintains that the combination of cited references fairly suggests the claimed invention, as stated in the last office action with regard to the excerpted portions of the references, and given the recognition by one of ordinary skill in the art of the value of tissue-specific expression of heterologous structural genes. With respect to Sengupta-Gopalan et al, Applicants' statements regarding the insufficiency of their teachings contradict Applicants' earlier statements on page 21 of the amendment of 28 June 2000, top paragraph. Thus, these two references taken together are not deficient, and the second rejection under 35 USC 103 which specifically addresses soybean as transformed plant host is also proper.**
>
> **Furthermore, Applicants' evidence of unexpected results, namely tissue-specific heterologous coding sequence expression under the control of a heterologous tissue-specific promoter, relies upon the use of three different tissue-specific promoters from three different *Brassica napus* genes. In contrast, the claims are broadly drawn to any tissue-specific promoter from any gene from any plant species. See In re Lindner, 173 USPQ 356 (CCPA 1972) and In re Grasselli 218 USPQ 769 (Fed. Cir. 1983) which teach that the evidence of nonobviousness should be commensurate with the scope of the claims.**

Applicants respectfully traverse the rejection of Claims 17-41, 43-48, 50-52 and 61-62 under 35 USC 103(a) as being unpatentable over Zambryski in view of Sengupta-Gopalan for all the reasons already made of record in the response submitted 21 June, 2000. As stated

above, Applicants do not agree with the Examiner's position. However, in the interest of furthering prosecution, have amended independent Claims 17, 18, 23, 28, 34, 39, 46, 52, 61 and 62 to recite a promoter or transcriptional initiation region from a gene of a *Brassica* plant. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the cited prior art. MPEP 2143.03. Zambryski discloses transferring T-DNA in the absence of internal T-DNA functions. The Examiner cites Zambryski for disclosing plasmids with a nopaline synthase promoter linked to antibiotic resistance genes. The Examiner proposes combining Zambryski with Sengupta-Gopalan, which discloses expressing β-phaseolin from *Phaseolus vulgaris* under the control of its native promoter. Sengupta-Gopalan does not teach or suggest any other promoter. Neither Zambryski nor Sengupta-Gopalan teach or suggest methods requiring the use of a promoter or transcriptional initiation region from a gene of a *Brassica* plant that is preferentially expressed in plant seed tissue, an element of the amended claims that the Examiner considers distinct (*see* pages 5-6 of paper 14). Therefore, Zambryski and Sengupta-Gopalan alone or in combination do not render obvious the claimed methods. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

Claims 20, 33, 38 and 41 remain rejected under 35 USC 103(a) as being unpatentable over Zambryski, et al taken with Sengupta-Gopalan et al, as applied to claims 17-41, 43-48, 50-52 and 61-62 above, and further in view of Pedersen *et al*, as stated in the last office action.

Applicants respectfully traverse this rejection, because including Pedersen does not cure the deficiencies of Zambryski and Sengupta-Gopalan. Pedersen discloses inducing crown galls in soybean plants, but does not teach or suggest anything about expressing a heterologous gene preferentially in plant seed tissue. The three combined references still do not teach or suggest methods using a promoter or transcriptional initiation region from a *Brassica* plant gene that is preferentially expressed in a plant seed tissue, an element the Examiner states is crucial to the claimed method (*see* page 5 of paper 14). Because each required element of the

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claimed methods is not taught or suggested by Zambryski, Sengupta-Gopalan and Pedersen, the Examiner is respectfully requested to withdraw this rejection.

> **Claims 17-41, 43-48 and new claims 50-52 and 61-62 are rejected under 35 USC 103(a) as being unpatentable over Hall, et al (US Patent 5,504,200) taken with Sengupta-Gopalan et al, as stated in the last office action for claims 17-32-34-37, 39-40 and 43-48.**
>
> **Applicants urge that the rejections under 35 USC 103 over Hall et al taken with Sengupta-Gopalan et al are improper, given the failure of Hall et al to teach a heterologous coding sequence, true seed-specificity, or resistance or degradation, the deficiencies of Sengupta-Gopalan et al as stated previously, and the failure of the additionally cited references in the second rejection to cure the deficiencies of the prior two references.**
>
> **The Examiner maintains that the combination of cited references fairly suggests the claimed invention, as stated in the last office action with regard to the excerpted portions of the references, and given the recognition by one of ordinary skill in the art of the value of tissue-specific expression of heterologous structural genes. Furthermore, Hall et al and Sengupta-Gopalan et al teach that the majority of phaseolin expression occurs in the seed, thus fulfilling the requirement of a seed-*preferential* promoter as claimed, and also fulfilling the art-recognized definition of a tissue-"specific" promoter as one which causes gene expression *primarily* in a particular tissue. The Examiner is unaware of a demonstration that Applicants' three exemplified promoters caused expression exclusively in seed tissue. With regard to product degradation, the Examiner maintains that seed storage proteins are normally degraded upon germination, as they are utilized for the nutrition of the germinating seedling.**
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> **With regard to Sengupta-Gopalan et al, the reference is not deficient as discussed above. Thus, these two references taken together are not deficient, and the second rejection under 35 USC 103 which specifically addresses soybean as the transformed plant host is also proper. Furthermore, see *Lindner* and *Grasselli* cited above.**

Applicants respectfully traverse the rejection of Claims 17-41, 43-48, 50-52 and 61-62 under 35 USC 103(a) as being unpatentable over Hall in view of Sengupta-Gopalan for all the reasons already made of record in the response submitted 21 June, 2000. As stated above, Applicants do not agree with the Examiner's position, but have amended the claims to recite a promoter or transcriptional initiation region from a *Brassica* plant in the interest of furthering prosecution. The disclosures of Hall and Sengupta-Gopalan are very similar: both disclose expressing β-phaseolin in tobacco plants under the control of its native phaseolin promoter. Neither teach nor suggest using any promoter other than the phaseolin promoter of *Phaseolus vulgaris*. Certainly, neither teach nor suggest any kind of method that requires a promoter or transcriptional initiation region from a *Brassica* plant gene that is preferentially expressed in plant seed tissue, an element the Examiner states is crucial to the claimed method (*see* page 5 of paper 14). Therefore, the combination of Hall with Sengupta-Gopalan as

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suggested by the Examiner can not teach or suggest every required element of the claimed methods, and the *prima facie* obviousness rejection is not proper. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

Claims 20, 33, 38 and 41 remain rejected under 35 USC 103(a) as being unpatentable over Hall, et al taken with Sengupta-Gopalan et al as applied to claims 17-41, 43-48, 50-52 and 61-62 above, and further in view of Zambryski et al taken with Pedersen *et al*, as stated in the last office action.

Applicants respectfully traverse the rejection of Claims 20, 33, 38 and 41 under 35 USC 103(a) as being unpatentable over Hall taken with Sengupta-Gopalan and further in view of Zambryski and Pedersen for all the reasons made of record in the response submitted on 21 June, 2000. As stated above, Applicants do not agree with the Examiner's position, but have amended the claims to recite a promoter or transcriptional initiation region from a *Brassica* plant in the interest of furthering prosecution. The further inclusion of Zambryski and Pedersen does not cure the deficiencies of Hall and Sengupta-Gopalan, because not one of these four cited references teaches or suggests a method requiring a promoter or transcriptional initiation region from a *Brassica* plant gene that is preferentially expressed in plant seed tissue, an element the Examiner states is crucial to the claimed method (*see* page 5 of paper 14). Therefore the *prima facie* obviousness rejection is not proper. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

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CONCLUSION

In view of the above amendment and remarks, it is submitted that this application is now ready for allowance. Early notice to that effect is solicited. If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (650) 328-4400.

Respectfully submitted,

Dated: 4 January, 2001

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Enclosures

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